has acceptable short-term survival, it is important to report longer outcome durations and delayed complications. In this report, retrospective analyses after transplantation from 2 centers from 1985 to 2003 were evaluated. Sixty-nine patients were evaluated, median age 33 years (16–75), 43 men and 26 women, 55 had nodular sclerosing HD, 7-lymphocyte predominant, 6-mixed cellular HD, and 1-unknown subtype. Conditioning regimens consisted of TBI/Cyclophosphamide in 11 patients, CBV in 38, BEAM/BEAC in 16, and Busulfan/Cyclophosphamide in 4. Forty-nine patients received peripheral stem cells (PSC), 17 received bone marrow (BM), and 3 received PSC plus BM. Seven patients (10%) had early mortality (<100 days) directly attributable to the transplant procedure. Four were cardiac-related and two due to infection. Long-term non-disease related mortality occurred in 16% secondary to MDS/AML, cardiac, respiratory, and infectious-related causes. Thirty-seven patients are alive, 30 patients have died, and 2 are lost to follow-up. The OS at 5 years was 49% and 21% at 10-years, respectively, while DFS at 5 years was 41% and 33% at 10 years, respectively, indicating that patients were dying of other causes late after transplantation. No difference in OS and DFS was noted according to disease status at transplantation (CR vs active disease), gender, or PSC vs BM. However, significant differences were noted in OS ($P < .05$) and DFS ($P < .05$) according to sensitivity to salvage therapy administered prior to transplantation. Achievement of CR after transplantation had a significant effect on OS. At the median follow-up of 32 months, the OS is 83%, with a predicted OS at 10 years of 68%. Failure to achieve CR after transplantation was associated with reduced OS, with 38% alive at 32 months, and all died by 10 years post-transplant. In conclusion, autologous transplantation offers a good long-term survival option for patients with relapsed/resistant HD. However, if CR is not attained after transplantation, alternative therapies should be pursued, because long-term outcomes for this patient group is dismal.

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AMIFOSTINE DOES NOT PROTECT AGAINST LIVER TOXICITY IN PATIENTS RECEIVING DOSE-ESCALATED IV BUSULFAN (IVBU) AND STANDARD DOSE CYCLOPHOSPHAMIDE IN AUTO BMT

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Eight adult patients undergoing autologous transplant for hematological malignancies were given a conditioning regimen of 4 daily single doses of IVBU followed 24 hours later by 2 days of cyclophosphamide (CP) at 60 mg/kg/day adjusted body weight. Amifostine 740 mg/m^2 was given just prior to each dose of IVBU and CP in an attempt to ameliorate toxicities and allow for IVBU dose-escalation. Dose-escalation of IVBU was based on AUC and was done in phase I fashion. There were 4 planned cohorts, with a targeted average daily AUC range for cohort 1 of 4400–5280 uMol-minute per day (midpoint 4800). This represents the AUC range commonly achieved by single daily doses of 3.2mg/kg/day. Each successive cohort of patients was to receive a dose of IVBU that would result in an AUC that was 20% greater than the previous group. Patients were given a test dose of 0.4 mg/kg of IVBU over 15 minutes between 7 and 21 days prior to conditioning. Pharmacokinetics (PK) performed around the test dose were used to base the first 2 conditioning doses of IVBU. Additional IVBU PK data was collected around conditioning doses 1and 3. If the targeted AUC range was not achieved based on the IVBU PK data for dose 1, IVBU doses were adjusted for days 3 and 4. Acetaminophen and metronidazole were held during all IVBU administration. Fungal prophylaxis was the same during IVBU test and conditioning doses. Patients received phenytoin for seizure prophylaxis. Five patients were enrolled in cohort 1. Three patients achieved the desired AUC for this cohort. The other 2 exceeded the target with AUCs that were within cohort 2 range. Despite this, there was no VOD and only grade 0 to 1 mucositis or diarrhea in this group. Three patients were enrolled in cohort 2 and met the targeted average daily AUC range of 5281–6340 uMol-minute per day (midpoint 5800) for that range. Two of 3 patients in cohort 2 developed late onset VOD (days +25, +22) and the protocol was closed. One of these patients died from complications of VOD. In cohort 2, there was 1 patient with grade 2 mucositis. Grade 0 to 1 mucositis and diarrhea was observed in the other patients. Amifostine appears to ameliorate mucositis and diarrhea in patients receiving standard doses of IVBU and CP in autologous BMT but does not protect against VOD in patients receiving dose-escalated IVBU at least when combined with CP.

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DURATION OF ULCERATIVE MUCOSITIS AND OUTCOMES OF AUTOLOGOUS (AU) HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOLLOWING HIGH-DOSE MELPHALAN (MP) CONDITIONING FOR MULTIPLE MYELOMA (MM)

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Background: OM is a common toxicity of conditioning regimens for HSCT that has been associated with adverse clinical and economic outcomes. **Methods:** A retrospective study of approximately 400 consecutive HSCT recipients was undertaken at a single academic center. Data were collected via chart review on days with ulcerative mucositis and selected outcomes including days with fever, days of parenteral narcotic therapy, incidence of Grade III or IV (Common Toxicity Criteria) infection, total inpatient days (LOS), and total inpatient charges. Data are reported here for the 115 MM patients who underwent AU HSCT after high-dose MP conditioning. **Results:** Mean age of study subjects was 54 years. Seventeen percent of patients received total body irradiation. Bone marrow was the source of most grafts. The relationship between duration of ulcerative mucositis and the outcomes of interest is reported below. **Conclusions:** Duration of ulcerative OM is associated with worse clinical and economic outcomes in MM patients undergoing AU HSCT following high-dose MP conditioning (Table1).

Table 1. *Outcomes of AU HSCT Following High-Dose Conditioning for MM, by Days with Ulcerative Mucositis*

	Days with Ulcerative Mucositis (Quartile)				
Outcomes	I n = 32	II n = 33	III n = 25	IV n = 25	P-value*
Fever days (mean,SD)	1.0 (1.9)	1.9 (3.2)	2.5 (2.5)	3.1 (3.7)	.0058
Narcotic therapy days (mean,SD)	0.7 (1.7)	3.9 (3.5)	4.4 (3.5)	8.8 (5.2)	<.0001
Infection (%)	10.0 (31.3)	10.0 (30.3)	12.0 (48.0)	9.0 (36.0)	.4115
LOS (mean,SD)	18.3 (3.1)	19.8 (3.5)	19.9 (3.4)	23.1 (3.5)	<.0001
Inpatient charges (mean,SD) (× 10,000)	11.7 (3.2)	12.3 (3.8)	11.8 (2.1)	15.5 (6.0)	.0016

*Test for linear trend; Cochran-Armitage for dichotomous and GLM for continuous measures.

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AUGMENTED HIGH DOSE CYCLOPHOSPHAMIDE, ETOPOSIDE, AND CARMUSTINE FOLLOWED BY TRANSPLANTATION WITH PERIPHERAL BLOOD STEM CELLS (PBSC) IN THE TREATMENT OF RELAPSED OR REFRACTORY HODGKIN'S DISEASE

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Introduction: The majority of patients with advanced stage Hodgkin's disease are cured with conventional dose combination chemotherapy. However, patients with disease that fails to enter a complete remission or that recurs after first-line chemotherapy have a poor prognosis. High dose chemotherapy with autologous stem cell transplantation is a highly promising treatment. We report the results of an augmented regimen containing cyclophosphamide, etoposide and carmustine followed by PBSC transplan-

tation. **Methods:** Patients with relapsed or refractory Hodgkin's disease received cyclophosphamide 4.5 g/m^2 for mobilization chemotherapy, following which they were given G-CSF 10 μg/kg/day subcutaneously until stem cell collection. Patients then received cyclophosphamide 1.8 g/m^2 from day −6 to day −3, etoposide 800 mg/m^{2}from day −6 to day −4, and carmustine 200 mg/m^2 on day −6 and day −5. Beginning on Day 0, G-CSF 5 μg/kg/day was administered. Patients with bulky disease at relapse or multiple (2 or more) recurrences in the same nodal basin(s) after primary or salvage therapies were eligible to receive consolidative radiotherapy. **Results:** 40 patients were enrolled in this study. Thirty-nine underwent autologous transplantation, with a median age of 31.8 years (range 17.5–74.4 years). Fifteen (37.5%) patients had primary refractory disease. The median times to neutrophil and platelet count recovery were 9 and 14.5 days, respectively. Twenty-two (55%) patients relapsed with a median time to progression of 0.98 years (range 0.2–8.7 years). Overall survival was 50% with a median follow up of 5.4 years (range 2–8.7 years). Four patients died of transplant related causes. These were: pulmonary fibrosis, adult respiratory distress syndrome, myocardial infarction prior to undergoing transplantation, and cryptogenic organizing pneumonitis (BOOP). **Conclusions:** Cyclophosphamide, etoposide, and carmustine is an effective high dose chemotherapy regimen for the treatment of relapsed and refractory Hodgkin's disease. However, many of these patients unfortunately relapse. Novel approaches to reduce the risk of relapse such as post transplant immunotherapy or allogeneic transplantation should be investigated in this patient population.

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HIGH DOSE MITOXANTRONE AND MELPHALAN FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION FOR LYMPHOID MALIGNANCIES

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We evaluated outcomes in 44 patients with lymphoid malignancies who underwent autologous stem cell transplantation following a preparative regimen of mitoxantrone 20 mg/m2 over 1 hour × 3 (total dose 60 mg/m2) and melphalan 60 mg/m2 over 1 hour × 3 (total dose 180 mg/m2). Twelve patients (6 male) had nodular sclerosing (n = 9) or mixed cellularity (n = 3) Hodgkin's Lymphoma (HL), while 32 patients (17 male) had diffuse large B-cell (n = 21), T-lymphoblastic (n = 4), mantle cell (n = 2), T cell rich B-cell (n = 1), or anaplastic large cell (n = 3) non-Hodgkin's lymphoma (NHL). The median age among Hodgkin's patients was 35 years (range 19–46 years) while the median age among NHL patients was 47 years (range 23–63 years). Two patients were in first complete remission (CR), 1 patient in CR2, while 15 patients had partial response, 14 patients had relapsed disease, and 12 patients had refractory disease at the time of transplant. All patients had a left ventricular ejection fraction of at least 40% at the time of transplant. Mitoxantrone and melphalan were well tolerated, with grade 3/4 mucositis the most common toxicity. Neutrophil engraftment was seen at the median of 13 days (range 8–34 days). Day 100 transplant related mortality (TRM) was 3%. The 3-year disease free (DFS) and overall survival (OS) were 63% and 67%, respectively. Three-year DFS were similar between HL and NHL patients (67% vs 63%: $P = .66$). There was no significant difference in 3-year DFS between patients with CR or PR versus relapsed or refractory disease (66% vs 62%: $P = .96$). DFS were similar among all disease subtypes. Congestive heart failure occurred in on 3 patients (7%). One patient died of complications from CHF while 2 others recovered cardiac function. In conclusion, mitoxantrone and melphalan preparative regimen is well tolerated with minimal cardiac toxicity in patients with lymphoid malignancies previously treated with anthracyclines.

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DIVIDED DOSE SCHEDULING OF MESNA TO PREVENT THE DEVELOPMENT OF CYCLOPHOSPHAMIDE-ASSOCIATED HEMORRHAGIC CYSTITIS IN AUTOLOGOUS TRANSPLANT PATIENTS

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Cyclophosphamide is an alkylating anti-neoplastic agent used for mobilization and transplant regimens in ASCT patients. Hemorrhagic cystitis (HC) is a possible adverse reaction associated with cyclophosphamide and may be prevented by the concomitant use of mesna and intravenous (IV) hydration. Several mesna dosing schedules have been studied in non-transplant clinical settings; however, few studies have included ASCT patients. In order to facilitate administration of cyclophosphamide in the outpatient setting, and to reduce hospitalizations for continuous bladder irrigation, the standard of care at our institution since January 2003 has been to give mesna IV at the same dose of cyclophosphamide in four equally divided doses at 15 minutes before, then 3, 6, and 8 hours after the administration of cyclophosphamide. A retrospective review was performed in ASCT patients to evaluate the effectiveness of this mesna dosing schedule with aggressive IV hydration in preventing the development of HC. Cyclophosphamide dosing in mobilization regimens was 3–4 gm/m2 and in transplant regimens was 60–120 mg/kg. Of the 64 patients evaluated, 35 (55%) developed hematuria according to NCI Common Toxicity Criteria, v. 3.0. Only one patient developed symptomatic HC. Four patients developed hematuria with concurrent urinary tract infections. There were no statistical differences between the groups who did or did not develop HC in terms of age, gender, underlying malignancy, past medical history, and concurrent use of medications that place a patient at increased hemorrhagic risk. More patients developed hematuria after receiving cyclophosphamide in transplant regimens than after mobilization regimens (24 vs 11 patients, $P \leq .05$). Patients who previously received cyclophosphamide or ifosfamide as conventional chemotherapy were more likely to develop hematuria ($P \leq .025$) after mobilization or conditioning regimens. Patients were more likely to develop hematuria after the transplant regimen if they had a prior history of receiving cyclophosphamide or ifosfamide ($P \leq .001$) with conventional or mobilization chemotherapy. In conclusion, mesna IV given in four equally divided doses with aggressive IV hydration is effective in preventing the development of significant HC. Additionally, this regimen facilitated the routine outpatient administration of high-dose cyclophosphamide.

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INTERLEUKIN 2 (IL-2) AND GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR (SARGRAMOSTIN) (GM-CSF) FOLLOWING AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANT (ASCT) FOR BREAST CANCER

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Relapse remains a major problem after autologous stem cell transplant for advanced breast cancer. GM-CSF has been shown in vitro to enhance IL-2 mediated tumor lysis. We evaluated if the addition of IL-2 and GM-CSF early after ASCT would reduce the risk for relapse and prolong survival, Between April 1998 and April 2002, 50 patients with inflammatory stage IIIB (n = 18) and chemo-responsive stage IV (n = 32) breast cancer were treated with high dose Busulfan (12 mg/kg), melphalan (100 mg/m^2), and Thiotepa (500 mg/m^2), followed by the infusion of autologous/syngeneic peripheral blood stem ells (PBSC). Thirty to 100 days after PBSC infusion after recovering from the acute toxicity of the myeloablative therapy, patients were scheduled to receive 12 weeks of IL-2 at 0.6×10^6 IU/m^2 sc daily and GM-CSF 125 ug/m^2 sc 3 times per week. All patients also took Tamoxifen 20 mg po qd during the 12 weeks of immunotherapy. Twenty-six (52%) patients